

What is claimed is:

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1. A method for improving thermostability of proteins, which comprises the steps of
(i) comparing amino acid sequences of proteins from two or more species which evolutionarily correspond to each other in a phylogenetic tree;
5 (ii) estimating an amino acid sequence of an ancestral protein corresponding to the amino acid sequences compared in step (i); and,
(iii) comparing the amino acid residues in the amino acid sequence in one of the proteins compared in step (i) with amino acid residues at a corresponding position in the ancestral protein estimated in step (ii), and replacing one or more amino acid residues of the protein different from those of the ancestral protein with the same amino acid residues as those of the ancestral protein.
 2. The method of claim 1, further comprising the steps of
(iv) testing the proteins obtained in step (iii) for thermostability; and
(v) selecting a protein having improved thermostability.
 3. A method for improving thermostability of proteins, which comprises the steps of
(i) comparing amino acid sequences of proteins from two or more species which evolutionarily correspond to each other in a phylogenetic tree by multiple alingment;
(ii) estimating an amino acid sequence of an ancestral protein corresponding to the amino acid sequences compared in step (i); and,
(iii) comparing the amino acid residues in the amino acid sequence in one of the proteins compared in step (i) with amino acid residues at a corresponding position in the ancestral protein estimated in step (ii), and replacing one or more amino acid residues of the protein different from those of the ancestral protein with the same amino acid residues as those of the ancestral protein.
 4. The method of claim 3, further comprising the steps of
(iv) testing the proteins obtained in step (iii) for thermostability; and
(v) selecting a protein having improved thermostability.
 5. The method for improving thermostability of protein according to claim 1, wherein
(a) thermophilic bacteria or archaebacteria are included in the species from which
the protein to be compared is derived in step (i); or

(b) two or more proteins belonging to the same family are included in the proteins to be compared in (i).

6. The method for improving thermostability of protein according to claim 3, wherein

(a) thermophilic bacteria or archaeobacteria are included in the species from which

5 the protein to be compared is derived in step (i); or

(b) two or more proteins belonging to the same family are included in the proteins to be compared in (i).

7. A protein improved in thermostability by the method of claim 1.

8. A Nucleic acid encoding the proteins of claim 7.

10 9. A recombinant DNA molecule containing the nucleic acids of claim 8 in a form being functional for expression.

10. A host cell having the recombinant DNA molecules of claim 9.

11. The method of claim 1, wherein the protein is an 3-isopropylmalate dehydrogenase.

12. The method of claim 1, wherein the protein is an isocitrate dehydrogenase.

13. The method of claim 1, wherein the maximum parsimony method is used for estimating an amino acid sequence of an ancestral protein.

14. The method of claim 3, wherein the maximum parsimony method is used for estimating an amino acid sequence of an ancestral protein.

15. The method of claim 1, wherein the neighbor-joining method is used for estimating an amino acid sequence of an ancestral protein.

16. The method of claim 3, wherein the neighbor-joining method is used for estimating an amino acid sequence of an ancestral protein.

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